

DOCKET NO.: CEPH-1157



COPY OF PAPERS  
ORIGINALLY FILED

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Robert L. Hudkins, et al.

Serial No.: 09/708,233

Group Art Unit: 2835

Filing Date: November 8, 2000

Examiner: Not Yet Assigned

For: SELECTIVE DERIVATIVES OF K-252a

DATE OF DEPOSIT: May 9, 2002

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231.

Wendy A. Choi  
TYPED NAME: Wendy A. Choi  
REGISTRATION NO.: 36,597

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

- ☒ In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first office action after the filing of request for continued examination under §1.114, no additional fee is required.

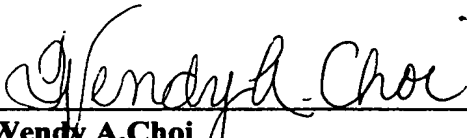
- ☐ In accordance with §1.129(a), this Information Disclosure Statement is being filed in connection with ☐the first or ☐second After Final Submission, therefore:
- ☐ Certification in Accordance with §1.97(e) is attached; or
- ☐ The fee of \$180.00 as set forth in §1.17(p) is attached.
- ☐ In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, or before an action that otherwise closes prosecution in the application, therefore:
- ☐ Certification in Accordance with §1.97(e) is attached; or
- ☐ The fee of \$180.00 as set forth in §1.17(p) is attached.
- ☐ In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); and the submission fee of \$180.00 as set forth in §1.17(p).
- ☐ Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.
- ☐ Copies of references listed on the attached Form PTO-1449 are enclosed herewith EXCEPT THAT:
- ☐ In view of the voluminous nature of references [list as appropriate], and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.

- ☒ In accordance with §1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. §120 have been made in the instant application:
- ☒ Copies of references [AA thru DK] listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior application Serial No. 08/867,084, filed June 2, 1997 .
- ☐ If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050.

This form is submitted in duplicate.

Date: May 9, 2002

  
**Wendy A. Choi**  
Registration No. 36,697

WOODCOCK WASHBURN LLP  
One Liberty Place - 46th Floor  
Philadelphia, PA 19103  
Telephone: (215) 568-3100  
Facsimile: (215) 568-3439



COPY OF PAPERS  
ORIGINALLY FILED

Sheet 1 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>CEPH-1157</b>	Serial No. <b>09/708,233</b>
		Applicant <b>Robert L. Hudkins, et al.</b>	
		Filing Date <b>November 8, 2000</b>	Group <b>2835</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	AA	Hirata, et al., "K-252 derivatives as protein C inhibitors, their preparation and formulation containing them", <i>Chemical Abstracts</i> , 111:728	
	AB	Abe, et al., "Arachidonic acid metabolis in Ischemic Neuronal Damage", <i>Annals of the New York Academy of Sciences</i> , 1989, 559, 259-268	
	AC	Borasio, "Differential effects of the protein kinase inhibitor K-252a on the in vivo survival of chick embryonic neurons", <i>Neuroscience Letters</i> , 1990, 108, 207-212	
	AD	Bozyczko-Coyne, et al., "A rapid fluorometric assay to measure neuronal survival in vivo", <i>Jrl of Neuroscience Methods</i> , 1993, 50, 205-216	
	AE	Tischler, et al., "A protein kinase inhibitor, staurosporine, mimics nerve growth factor induction of neurotensin/neuromedin N gene expression", <i>The Journal of Biological Chemistry</i> , 1991, 266, 1141-1146	
	AF	Vitullo, Press Release "Cephalon and Kyowa Hakko Co., Ltd. Announce Collaboration", <b>June 2, 1992</b>	
	AG	Wolf, G. et al., "The protein kinase inhibitor staurosporine, like phorbol esters, induces the association of protein kinase C with membranes", <i>Biochem. And Biophys. Research Communication</i> , 1988, 154, 1273-1279	
	AH	Wenk, G. et al., "Nucleus basalis magnocellularis: optimal coordinates for selective reduction of choline acetyltrans-ferase in frontal neocortex by ibotenic acid injections", <i>Exp. Brain Res.</i> , 1984, 56, 335-340	
	AI	Chiu, A. et al., "A motor neuron-specific epitope and the low affinity nerve growth factor receptor display.. Development, Axotomy and Regeneration", <i>Jrl of Comparative Neurology</i> , 1993, 328, 351-363	
	AJ	Chu-Wang, et al., "Cell death of motoneurons in the chick embryo spinal cord", <i>J. Comp. Neur.</i> , 177, 33-58	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

RECEIVED

JUN 05 2002

TECH CENTER 2800



COPY OF PAPERS  
ORIGINALLY FILED

Sheet 2 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>CEPH-1157</b>	Serial No. <b>09/708,233</b>
		Applicant <b>Robert L. Hudkins, et al.</b>	
		Filing Date <b>November 8, 2000</b>	Group <b>2835</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	AK	Davis, et al., "Potent selective inhibitors of protein kinase C" <i>FEBS Letters</i> , 1989, 259, 61-63	
	AL	Davis, et al., "Inhibitors of protein kinase C.1 1 2,3-Bisarylmaleimides", <i>J. Med. Chem.</i> , 1992, 35, 177-184	
	AM	Dunnett, S. et al., "The basal forebrain-cortical cholinergic system: interpreting the functional consequences of excitotoxic lesions", <i>TINS</i> , 1991, 14, 494-501	
	AN	Fibiger, H., "Cholinergic mechanisms in learning, memory and dementia; a review of recent evidence", <i>TINS</i> , 1991, 14, 220-223	
	AO	Glicksman, M. et al., "K-252a and staurosporine promote choline acetyltransferase activity in rat spinal cord cultures", <i>J. of Neurochemistry</i> , 1993, 61, 210-221	
	AP	Glicksman, M. "K-252a Molecules as Promoters..." Third Int. Conference on Nerve Growth Factor (NGF) and related molecule, Chateau Lake Louise, Lake Louise, Alberta, Apr-May 1, 1994	
	AQ	Glicksman, M. et al., "K-252a promotes survival of striatal neurons in culture", <i>Society of Neuroscience abstracts</i> , 1993, 96:680	
	AR	Hamburger, "Cell death in the development of the lateral motor column of the chick embryo", <i>J. Comp. Neur.</i> , 1975, 160, 535-546	
	AS	Hara, et al., "Staurosporine, a novel protein kinase C inhibitor, prevents postischemic neuronal damage in the gerbil and rat", <i>J. of Cerebral Blood Flow and Metabolism</i> , 1990, 10, 646-653	
	AT	Hashimoto, et al., "Staurosporine-induced Neurite outgrowth in PC12h Cells", <i>Experimental Cell Research</i> , 1989, 184, 351-359	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

RECEIVED

JUN 25 2002

TECH CENTER 2800



COPY OF PAPERS  
ORIGINALLY FILED

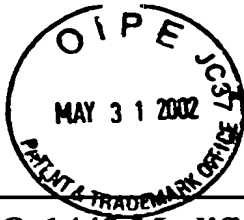
Sheet 3 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>CEPH-1157</b>	Serial No. <b>09/708,233</b>
		Applicant <b>Robert L. Hudkins, et al.</b>	
		Filing Date <b>November 8, 2000</b>	Group <b>2835</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	AU	Hashimoto, "K-252a, a potent protein kinase inhibitor, blocks nerve growth factor-induced neurite outgrowth and changes in the phosphorylation of proteins in PC12h cells", <i>J. Cell Biology</i> , 107, 1531-1539	
	AV	Kase, et al., "K-252a, A protein inhibitor of protein kinase C from microbial origin", <i>The Jrl of Antibiotics</i> , 1986, 39, 1059-1065	
	AW	Kiyoto, et al., "Staurosporine, a potent protein kinase.. Caused ornithine decarboxylase induction in isolated mouse epidermal cells", <i>Biochem. and Biophys. Research Communications</i> , 1987, 148, 740-746	
	AX	Knuet, et al., "K-252b is a selective and nontoxic inhibitor of nerve growth factor action on cultured brain neurons", <i>Jrl. of Neurochemistry</i> , 1991, 57, 955-962	
	AY	Knusel, et al., "K-252b selectively potentiates cellular actions and trk tyrosine phosphorylation mediated by neurotrophin-3" <i>Jrl. of Neurochemistry</i> , 1992, 59, 715-722	
	AZ	Koizumi, et al., "K-252a; A specific inhibitor og the action of nerve growthfactor in PC12 cells", <i>The Jrl. of Neuroscience</i> , 1988, 8, 715-721	
	BA	Lazarovici, et al., "K-252a inhibits the increase in c-fos transcription and the increase in intracellular calcium produced by nerve growth factor in PC12 cells", <i>Jrl. of Neuroscience Research</i> , 1989, 23, 1-8	
	BB	McManamann, J. et al., "Rescue of motoneurons from cell death by a purified sketetal muscle polypeptides: effects of the ChAT development factor in PC12 cells", <i>Neuron</i> , 1990, 4, 891-898	
	BC	Matsuda, et al., "The effect of K-252a, A potent microbial inhibitor of protein kinase, on activated cyclic nucleotide phosphodiesterase", <i>Biochem J.</i> , 1988, 256, 75-80	
	BD	Moody, et al., "synthesis of the staurosporine aglycon", <i>J. Org. Chem.</i> , 1992, 57, 2105-2114	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

RECEIVED

JUN 05 2002

TECH CENTER 2800



COPY OF PAPERS  
ORIGINALLY FILED

Sheet 4 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>CEPH-1157</b>	Serial No. <b>09/708,233</b>
		Applicant <b>Robert L. Hudkins, et al.</b>	
		Filing Date <b>November 8, 2000</b>	Group <b>2835</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	BE	Morioka, et al., "Staurosporine-induced differentiation in a human neuroblastoma cell line, NB-1", <i>Agric. Biol. Chem.</i> , 1985, 49, 1959-1963	
	BF	Nabeshima, et al., "Staurosporine, a protein kinase inhibitor, attenuates basal forebrain-lesion-induced amnesia and cholinergic neuronal deficit", <i>Neuroscience Letters</i> , 1991, 122,13-16	
	BG	Nabeshima, et al., "Staurosporine facilitates recovery form the basal forebrain-lesion-induced...Cholinergic neuron in rats", <i>The Jrl of Pharmacology and Experimental Therapeutics</i> , 1991, 257, 562-566	
	BH	Nakadate, et al., "Comparasion of protein kinase C functional assays to clarify mechanisms of inhibitor action", <i>Biochemical Pharmacology</i> , 1988, 37, 1541-1545	
	BI	Nakanishi, et al., "K-252b,c and d, potent inhibitors of protein kinase c from microbial origin", <i>The Jrl of Antibiotics</i> , 1986, 39, 1066-1071	
	BJ	Ohno, et al., "Effect of staurosporine, a protein kinase C inhibitor, on impairment of working memory in rats exposed ot cerebral ischemia", <i>European Jrl of Pharmacology</i> , 1991, 204, 113-116	
	BK	Olton, D. et al., "Dementia: Animal models of the cognitive impairments...Cholinergic system", <i>Psychopharmacology: The third Generation of Progress</i> , Raven Press, NY, 1987	
	BL	Oppenheim, "The absense of significant paotnatal motoneuron death in the brachial and lumbar spinal cord of the rat", <i>Jrl. of Comparative Neurology</i> , 1986, 246, 281-286	
	BM	Oppenheim, R. et al., "Cell death of motoneurons in the chick embryo spinal cord, VQ. Reduction of naturally occurring cell death...Terni by nerve growth factor", <i>Jrl of Comparative Neurology</i> , 1982, 210, 174-189	
	BN	Rasouly, et al., "Staurosporine-induced neurite outgrowth in PC12-Cells is independant of protein kinase-C Inhibition", <i>Molecular Pharmacology</i> , 1991, 42, 35-43	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

RECEIVED

JUN 05 2002

TECH CENTER 2800



COPY OF PAPERS  
ORIGINALLY FILED

Sheet 5 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>CEPH-1157</b>	Serial No. <b>09/708,233</b>
		Applicant <b>Robert L. Hudkins, et al.</b>	
		Filing Date <b>November 8, 2000</b>	Group <b>2835</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	BO	Sako, et al., "Contrasting actions of staurosporine, a protein kinase C inhibitor, on human neurophils and primary mouse epidermal cells", <i>Cancer Research</i> , 1988, 48, 4646-4650	
	BP	Shea, et al., "Staurosporine-induced morphological differentiation of human neuroblastoma cells", <i>Cell Biology International Reports</i> , 1991, 15, 161-167	
	BQ	Shepherd, "The synaptic organization of the brain" Second Edition, Oxford University Press, New York, 1979, 308-314	
	BR	Siman, et al., "Excitatory amino acids activate calpain I and induce structural protein breakdown in vivo", <i>Neuron</i> , 1988, 1, 279-287	
	BS	Slack, et al., "Effects of retinoic acid and staurosporine on the protein kinase C activity and the morphology of two related human neuroblastoma cell line", <i>Biochimica et Biophysica Acta</i> , 1990, 1053, 89-96	
	BT	Smith, G. "Animal models of Alzheimer's disease: experimental cholinergic denervation", <i>Brain Research Reviews</i> , 1988, 13, 103-118	
	BU	Smith, et al., "Effects of protein kinase C inhibitor, K-252a, on human polymorphonuclear neutrophil responsiveness", <i>Biochem. And Biophys. Reserach Communication</i> , 1988, 152, 1497-1503	
	BV	Steglich, et al., "Indole pigments from the fruiting bodies of the slime mold <i>Arcyria denudata</i> ", <i>Agnew. Chem. Int. Ed. Engl.</i> , 1980, 19, 459-460	
	BW	Knusel, et al., "K-252 compounds: Modulators of Neurotrophin signal transduction", <i>Jrl. of Neurochemistry</i> , 1992, 59, 1987-1996	
	BX	Beal, et al., "Alzheimer's disease and other dementias", <i>Harrisons's Principles on Internal Medicine</i> , Isselbacher, et al., eds., McGraw-Hill Inc., New York, 2272-2273	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

RECEIVED

JUN 05 2002

TECH CENTER 2800



COPY OF PAPERS  
ORIGINALLY FILED

Sheet 6 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>CEPH-1157</b>	Serial No. <b>09/708,233</b>
		Applicant <b>Robert L. Hudkins, et al.</b>	
		Filing Date <b>November 8, 2000</b>	Group <b>2835</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	BY	Brouillet, et al., "Chronic mitochondrial energy impairment produces selective striatal degeneration and...", <i>Proc. Natl. Acad. Sci</i> , <b>1995</b> , 92, 7105-7109	
	BZ	Mallamo, J.P. et al., "Conformationally restricted analogues of disoxaril: a comparasion of the activity against human rhinovirus type 14 and 1A", <i>J. Medicin. Chem.</i> , <b>1992</b> , 35(25), 4690-4695	
	CA	Ross, A.H. et al., "Differential biological effetcs of K252kinase inhibitors are related to membrane solubility but not to permeability", <i>J. Neurochem</i> , <b>1995</b> , 65(6), 2748-2756	
	CB	Containing Them, chemical Abstracts 111:728, XP002041235 see abstract and 12 <sup>th</sup> Collective Chemical Substance Index, p 34237	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

RECEIVED

JUN 05 2002

TECH CENTER 2800



COPY OF PAPERS  
ORIGINALLY FILED

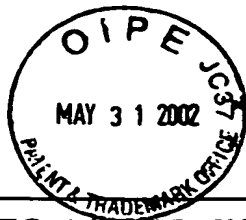
Sheet 7 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office				Docket No. <b>CEPH-1157</b>		Serial No. <b>09/708,233</b>	
				Applicant <b>Robert L. Hudkins, et al.</b>			
				Filing Date <b>November 8, 2000</b>		Group <b>2835</b>	
<b>U. S. PATENT DOCUMENTS</b>							
<b>Examiner Initial</b>		<b>Document No.</b>	<b>Date</b>	<b>Name</b>	<b>Class</b>	<b>Subclass</b>	
	CC	4,554,402	11/19/85	Hawkins, et al.			
	CD	4,735,939	04/05/88	McCoy, et al.			
	CE	4,816,450	03/28/89	Bell, et al.			
	CF	4,877,776	10/31/89	Murakata, et al.			
	CG	4,923,986	05/08/90	Murakata, et al.			
	CH	5,043,335	08/27/91	Kleinschroth, et al.			
	CI	5,093,330	03/03/92	Caravatti, et al.			
	CJ	5,344,926	09/06/94	Murakata, et al.			
	CK	5,461,145	10/24/95	Kudo, et al.			
	CL	5,461,146	10/95	Lewis, et al.	540	545	
	CM	5,468,872	11/95	Glicksman, et al.	548	416	
	CN	5,516,771	05/14/96	Dionne, et al.			
	CO	5,516,772	05/96	Glicksman, et al.	514	211	
	CP	5,621,100	04/97	Lewis, et al.			
<b>EXAMINER</b>				<b>DATE CONSIDERED</b>			

RECEIVED

JUN 05 2002

TECH CENTER 2800



COPY OF PAPERS  
ORIGINALLY FILED

Sheet 8 of 8

<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office	Docket No. <b>CEPH-1157</b>	Serial No. <b>09/708,233</b>
	Applicant <b>Robert L. Hudkins, et al.</b>	
	Filing Date <b>November 8, 2000</b>	Group <b>2835</b>

**FOREIGN PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Country	Translation	
					YES	NO
	CQ	AU-A 17571/88	12/15/88	Australia		
	CR	EP 0 238 011 A2	09/23/87	EPO		
	CS	EP 0 296 110 A3	12/21/88	EPO		
	CT	EP 0 323 171 A3	07/05/89	EPO		
	CU	EP 0 370 236 A1	05/30/90	EPO		
	CV	EP 0 558 962 A1	09/08/93	EPO		
	CW	EP 0 630 898 A1	12/94	EPO		
	CX	JP 62 120 388	06/01/87	Japan		
	CY	JP 62 155 284	07/10/87	Japan		
	CZ	JP 62 155 285	07/10/87	Japan		
	DA	JP 63 295 588	12/01/88	Japan		
	DB	JP 63 295 589	12/01/88	Japan		
	DC	JP 5 086 068	04/06/93	Japan		
	DD	JP 5 247 055	09/24/93	Japan		
	DE	JP 6 073 063	03/15/94	Japan		
	DF	WO 88/07045	09/88	PCT		
	DG	WO 89/07105	08/89	PCT		
	DH	WO 91/09034	06/27/91	PCT		
	DI	WO 93/08809	05/13/93	PCT		
	DJ	WO 94/02488	02/03/94	PCT		
	DK	WO 95/00520	01/05/95	PCT		

**EXAMINER**

**DATE CONSIDERED**

**RECEIVED**

JUN 05 2002

TECH CENTER 2800